RESEARCH ARTICLE

ESTABLISHING NATIONAL GUIDELINES FOR EARLY DETECTION OF BREAST CANCER IN IRAQ: Clinical Implications and Perspectives

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Manuscript Info	*Abstract*
	In addition to being the most important cancer, breast cancer is often associated with other features that threaten lives of women in Iraq. Studies have documented an exponential rise in the incidence rates of the disease, the prevalence of younger ages and advanced stages at the time of presentation. Mortality estimates displayed that breast cancer is responsible for the highest rate of deaths from malignancies among Iraqi females. The lack of strategic well designed diagnostic policies and inadequate treatment facilities lead to significantly low five-year survival rates from the disease in Iraq as compared to high-income countries. The outcomes of the Iraqi studies obviously illustrate significant knowledge gaps regarding the relative significance of diagnosing breast cancer in the community and suggest a potential to take practical policy decisions that aim at elevating the level of awareness among Iraqi women The aforementioned findings justify as well increasing efforts for establishing feasible breast cancer control programs in Iraq focusing provisionally on promoting early detection nationwide. A decision to implement screening as part of a cancer control strategy in our country should be preceded by promoting evidence-based guidelines for educating both the public and health care professionals. The present paper demonstrates the clinical implications and perspectives of establishing national guidelines for the early detection of breast cancer in Iraq.

Introduction

Iraqi Cancer Statistics

Cancer has become a major public health problem; its burden rising with the increase in population size (1). It is the leading cause of death among the Iraqi population following cardiovascular diseases. The latest Iraqi Cancer Registry (ICR) reveals that among an estimated population size of 32, 500000, a total of 20, 278 new cases of cancer were registered among Iraqis in 2011; 9,352 were diagnosed in males with an incidence rate of 55 /100 000 population, while 10,926 affected females with an incidence rate approximating 67/100 000 population (2).

Breast Cancer

Worldwide, breast cancer is the most commonly diagnosed malignancy among women (1). In Iraq, it ranked the first cancer among the Iraqi population since 1986 till the present time; the number of registered cases being double that recorded for lung cancer. In 2011, the ICR reported 3,845 cases of breast cancer in both genders accounting for

about 19% of all newly diagnosed cancers. Of those 3,763 were among females forming 34.4% of the registered female cancers with an incidence rate approximating 23/100,000 female population (2). The highest incidence rate is often observed in middle aged females in the age group (45-49) years; while the peak age specific incidence rate is displayed   in the age group (50-54) years (2,3).

Significance of initiating Breast Cancer Early Detection Programs in Iraq and the Eastern Mediterranean Region (EMR)

In addition to being the most important cancer, breast cancer in EMR is often associated with other features that threaten lives of women. These include the exponential annual rise in the incidence rates of the disease, the higher frequencies of presentation at younger age groups and the advanced stages at the time of diagnosis (3,4). In addition, there is a likely prevalence of more aggressive tumour behavioural forms (1,3,5). These factors lead to low five-year survival rates (10- 50%) from breast cancer in many low- and middle- resource countries as compared to 85% and over in high-income settings (1,6).

In Iraq, it has been reported that 19.8% of women presenting with palpable breast lumps, in a major screening center for early detection of breast cancer, were diagnosed with breast cancer. Interestingly, about 90.6% of those patients detected the lumps by themselves; nevertheless, only 32% sought medical advice within the first month, while 16.% consulted a doctor one year later. Approximately one third of those patients presented in the age group (40–49 years), 16% had a positive family history and 47% were diagnosed at advanced stages (3).
In another survey which was conducted to explore the knowledge, attitude and practice towards breast cancer among a sample of educated Iraqi women, it was demonstrated that approximately half of the participants had low knowledge score (less than 50%). The same study revealed that 90% of the respondents had heard about Breast Self-Examination (BSE), however, only 43% did actually practice the technique (7). In a similar study carried out in the North of Iraq, multiple logistic regressions displayed that the age of the participants and their knowledge on the means of early detection of breast cancer and its risk factors were significantly associated with practicing BSE (8). The outcomes of those studies obviously illustrate significant knowledge gaps about the relative importance of breast cancer in the community and suggest a potential to take practical policy decisions that aim at increasing early detection through elevating the level of awareness among Iraqi women (9).

Regarding mortality, it has been estimated that breast cancer is responsible for the highest rate (23%) of deaths from malignancies among Iraqi females (1,6). The World Health Organization (WHO) documented that early detection and screening, when coped with appropriate therapy, could offer a reduction in breast cancer mortality; displaying that the poor survival in less developed countries, including Iraq, is mainly attributed to the lack of strategic well designed diagnostic policies and inadequate treatment facilities (4, 10, 11). The aforementioned findings justify increasing efforts for establishing feasible comprehensive breast cancer control programs in Iraq focusing provisionally on promoting early detection nationwide.

Early Detection of Cancer: Definition of Terms

Early detection is part of a wider strategy that includes diagnosis, treatment of the condition detected, and follow-up. The aim is to detect a cancer when it is localized before invasion to surrounding tissues and distant organs. It is the second major component of National Cancer Control Programs, the first being prevention `Worldwide, about a third of all cancers are amenable to early detection and potential cure with effective treatment (4, 9, 10). Without early detection, treatment resources are used inefficiently and the need for palliative care services increases unnecessarily. A decision to implement early detection of cancer as part of a cancer control strategy in a country should be evidence-based, depending on the burden of the disease, the efficacy and cost-effectiveness of the early detection manpower requirements and the level of development of health services (4, 10, 11).
An early detection program is the organized and systematic implementation in a defined population of early diagnosis or screening (or both). **Accordingly, there are two principal components of Early Detection programs for Cancer – Early Diagnosis and Screening** (10, 11):
Early Diagnosis*:* is the awareness by the public and health professionals of the early signs and symptoms of cancer to facilitate diagnosis and offer simpler effective therapy (Down Staging of Cancer). That could be achieved through promoting health education.

Screening*:* is the systematic application of a non-invasive simple screening test in a presumably asymptomatic target population to identify individuals with an abnormality suggestive of a specific cancer. *Opportunistic Screening* is the unsystematic application of screening tests in health services.

A screening program is more complex than an early diagnosis program. In the latter an effective screening test needs to be applied to over 70% of the target population at risk in order to achieve a major effect on mortality from the cancer in question. All the necessary infrastructure and resources have to be in place for offering the test periodically. Because tumour size predicts long-term survival among women with lymph node-positive breast cancer (12), the size of the tumour has to be an important objective of our early detection programs, i.e., to ensure that Iraqi women present with breast cancer at the smallest possible detectable size.

Initiating Public Awareness Campaigns and Early Detection Programs to Control Breast Cancer in Iraq:

Promoting simple early detection policies for the control of breast cancer in Iraq should be accompanied by initiating comprehensive evidence based public health education campaigns. It is mandatory to establish massive nationwide programs for raising the awareness of the female population on the signs and symptoms of breast cancer, its risk factors and the recommended approaches for the prevention and early detection of the disease. These campaigns should focus on the crucial benefits of diagnosing lumps at their earliest stages and abiding to the early detection protocols (9, 13). Within that context, the Ministry of Health (MoH) and Ministry of Higher Education and Scientific Research (MoHESR) have already initiated active steps to promote early detection and public health awareness among the Iraqi women (13).

The MoH "National Program for Early Detection and Down Staging of Breast Cancer" In Iraq:

In 2000, a National Program for Early Detection and Down Staging of Breast Cancer was initiated by the Ministry of Health (MoH) in collaboration since 2000. Referral centres and specialized clinics for early detection of breast cancer were established in all 18 governorates. The work started in 4 main specialized centres (Baghdad (2), Basrah, Ninawa) in addition to 16 specialized clinics for early detection of breast cancer in the major hospital of each governorate in Iraq. Within these centres and clinics, breast cancer early detection techniques are promoted including: Physical Breast Examination (PBE), Breast Self Examination (BSE), Mammography, Ultrasonography (U/S) and Fine Needle Aspiration Cytology (FNAC).

The main objectives of that ongoing program are:
- Down staging breast cancer at the time of presentation in Iraq, where opportunities for cure are higher.
- Promoting public awareness on the risk factors of breast cancer, signs and symptoms of the disease and available screening tools.
- Reducing the financial burden of breast cancer management.
- Decreasing the morbidity and mortality rates of breast cancer – as long term objectives.

That national early detection program, supervised by MoH, has a national policy and protocols and follows a multidimensional approach to achieve its goals represented in ensuring provision of high quality diagnostic and treatment services and capacity building of the health staff working in this field in addition to encouraging public health education of the Iraqi women. The program plan of action has been expanded both horizontally and vertically and at the present time it has incorporated the primary health care sector.

The MoHESR "Iraqi National Breast Cancer Research Program" (14):

To address the aforementioned information needs on the clinical profile of breast cancer patients, and emphasizing the role of research as one of the basic pillars in the adoption of the cancer control strategy, "Iraqi National Breast Cancer Research Program" (INBCRP) was established by the Iraqi MoHESR in 2009.   In collaboration with the International Agency for Research on Cancer (IARC) and WHO/EMRO, the Iraqi researchers developed a comprehensive information system data base to document the demographic characteristics, clinico-pathological presentations and management outcomes of Iraqi patients diagnosed with breast cancer (13, 14)**.**

Strategic Target of the INBCRP (14)

- Promoting Research on the topics of breast cancer control.
- Conducting comparative demographic and clinic-pathological research studies on the behaviour of breast cancer in the region.
- Establishing breast cancer information system data base.

- Raising awareness of the general population to the common signs and symptoms of cancer in general and breast cancer in particular.
- Updating knowledge and upgrading skills through training of the health care professionals working in the fields of breast cancer screening and control.
- Strengthening counseling skills

In order to accomplish the strategic targets of the INBCRP and aiming to support the provision of relevant health services to the Iraqi women, a **"Breast Cancer Research Unit"** was established in 2010 in Baghdad University Medical College. That Unit was in charge of implementing the objectives of the national cancer research program and supervising all the relevant activities that were executed by the program follow-up committees at the level of each Iraqi governorate. Membership of those specialized committees comprises Professors and experts in the fields of Pathology, Radiology, Surgery, Public Health, Gynecology, Oncology and Nursing. The Research Unit was promoted to the level of a **"National Cancer Research Center"** in 2012 following the endorsement of the Scientific Research Board authority of the MoHESR.

In January 2012, WHO/EMRO in collaboration with the Iraqi National Cancer Research Center, IARC, Susan G Komen for the Cure Organization and IAEA/PACT - organized a "Consultative Meeting" to discuss the plan of action for implementing a "Regional Comparative Breast Cancer Research Project in the EMR" (Sharm Al-Sheikh, Cairo) utilizing the established Iraqi breast cancer data base (13). The roles of the international collaborating agencies in that project were clearly defined and the expected outcomes of that regional program were illustrated. The "online" information system data base, supervised by the Screening Group of IARC, is currently operating in specified major cancer facilities within the Arab region i.e., Iraq (National Cancer Research Center/ Baghdad University), Egypt (National Cancer Institute/Cairo University), Jordan (King Hussein Cancer Center) and Lebanon (Lebanese Cancer Society).

Diagnostic Approaches to Breast Lesions:

Although mammography machines, as main screening tools for breast cancer, are available in the major hospitals in each province in Iraq, yet those are mainly used for diagnostic purposes in patients who present with palpable breast lumps. Obviously, due to cost effective measures and the economical challenges that Iraq is facing, it is not expected that the authorities could provide mammography devices across every health care centre in the country to be used for screening of all Iraqi women. Other obstacles include the lack of resources illustrated in the inadequate number of well trained radiologists and radiographers coupled by the insufficient standardized quality control procedures. That urges the necessity to promote other feasible screening tools to support in diagnosing breast cancer.

History and Case Recording:

A thorough comprehensive history is mandatory. The National Program for Early Detection of Breast Cancer organized "Case Sheet File Questionnaires" that are utilized in its Referral Centers and Specialized Clinics all over the Iraqi provinces, for documenting all relevant data. The assessed parameters include demographic profile, age at diagnosis, marital status, educational level, age at first delivery, age at menarche, number of parity, family history of the disease, history of previous breast diseases, lactation or hormonal intake. All findings of clinical examinations and results of diagnostic (imaging and laboratory) investigations are recorded for follow-up (13).

Clinical Breast Examination (CBE)

This is an inexpensive, simple non-invasive method of early detection performed by a trained health care provider (usually a physician or a nurse) that aims to detect breast abnormalities in their earliest stage of presentation, Studies have shown that CBE alone detected 3%–5% of breast cancers that are missed through screening mammography in women over the age of 50, and 10% or more in women aged 40–49 (15); the majority were tumours measuring more than 2 cm in diameter. Although degrees of competence, profession and thoroughness vary, it has been reported that approximately 80-90% of breast cancer cases in Iraq are usually found either by the patient herself (5, 16) or by the examining physician through CBE.

The Breast Health Global Initiative (BHGI) Summit Guidelines for breast health care recommended CBE as a screening measure of choice to be employed for early detection of breast cancer in countries with limited recourses where breast cancer is often diagnosed at advanced stages at the time of presentation (18). However, in our practice,

the findings of CBE cannot be used alone to give a definite diagnosis of malignancy, without the information provided through diagnostic mammography and tissue biopsy (i.e., Triple Assessment Test) (5, 19).

Procedure of CBE (10, 15-17):

The efficacy of CBE is dependent upon a number of factors that include proper positioning of the patient, thoroughness of the search and accurate movement of the fingers on each breast for a duration of 5 minutes. The patient should be examined in both the upright and supine positions. She must be disrobed from the waist up allowing the examiner to visualize the breasts thoroughly.

Inspection: Should be performed while the patient assumes three standing positions: arm relaxed at the sides, hands pressed firmly on the waist (to contract the pectoral muscles) and arms over the head allowing the lower part of the breast to be inspected.

The examiner should look for:

➢ Changes in color of the skin: darkness, redness or abnormal vascularity
➢ Swelling, asymmetry or changes in breast contour: size or shape
➢ Dimpling or puckering of the skin
➢ Changes in the nipples redness, excoriation, crust, retraction or abnormal direction
➢ Spontaneous nipple discharge specifically if bloody
➢ "Orange peel" appearance of the breast skin.

Palpation: Should be carried out using the palmer aspect of the three middle fingers. The examination should cover the whole area of each breast including the axillary region and the upper chest; moving from the collar bone to below the breasts and from the armpits to the breastbone; searching in vertical, circular or wedge patterns (Figure 1). It is advisable to record the location of any abnormality by documenting the position on the breast and the distance in centimeters from the areola.
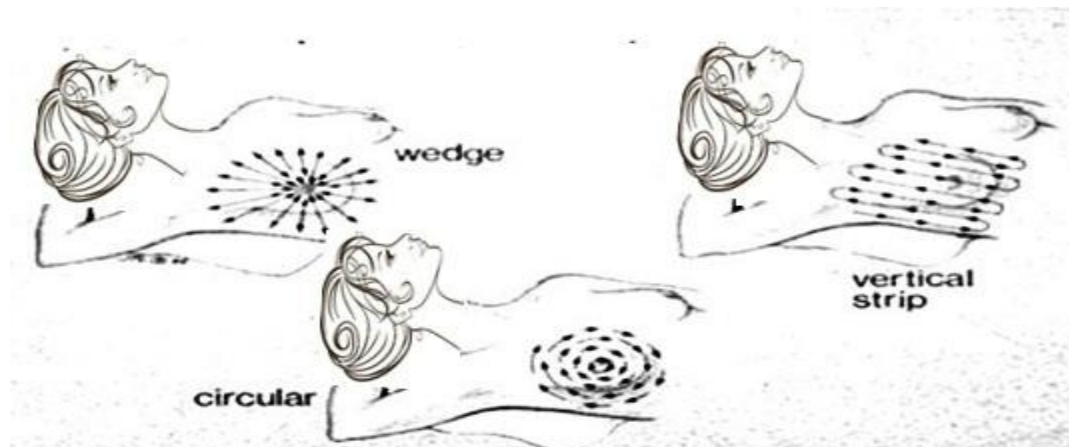
Figure (1): Breast Palpation Techniques.

Any thickening, knots, modularity or lump which has not been noted previously during earlier examinations should be investigated thoroughly. It is very helpful to record the location of any abnormality by documenting both the position on the breast and the distance in centimeters from the areola. In this manner, the precise location can be easily identified on subsequent follow-up examinations. The nipple should then be squeezed gently for any abnormal discharge.

Integrating CBE with Mammography:

Earlier surveys demonstrated that the sensitivity and effectiveness of the two diagnostic approaches when combined together was higher than when each was conducted separately, specifically in young women under 40 years (16, 17, 20).. WHO (10, 15) and the American cancer society (ACS) (17) recommends women after the age of 40 years to do both examinations every year; CBE to be conducted before mammography, to attract the attention of the examining radiologist to any abnormal finding detected by CBE.

Recommendations:

The International Guidelines recommend CBE to be performed at least every 3 years starting in the age group (20 - 39 years) and annually starting at the age of 40 years (4, 10, 16, 19, 20).

In Iraq, as a low middle income country, the resources for establishing a fully equipped nationwide early detection system for the target population at risk are limited. CBE is recommended as a feasible cost effective approach for detecting breast lumps specifically in young and premenopausal women; where the peak frequency of breast cancer is demonstrated and where the mammograms are less sensitive. Thus, Iraqi Physicians are expected to perform CBE for women starting at the age of 20 years, as a part of her routine check-up every 2-3 years, increasing to once a year from the age of 30. Women at high risk of breast cancer should be encouraged to have annual BSE after the age of 25. Once an abnormality is detected, the patient should be referred for mammography and other relevant diagnostic investigations.

Breast Self-Examination (BSE):

The purpose of BSE is to urge women to learn the topography of their breasts, in order to identify future changes. BSE should be used in combination with mammography and CBE, and not as a substitute for either method. According to the National Breast Cancer Foundation, USA (22) up to 70% of breast cancers are found by women performing their own BSE. Although there is no evidence based data to support the efficacy of BSE as a screening modality (15, 17, 20, 21), nevertheless, it is internationally agreed that all women should be urged to learn how their breast normally look and feel in order to report any changes promptly to their health care provider (15, 17, 18, 20, 21). It is indicated that BSE is a good option for women starting in their twenties.

Our Iraqi data revealed that about 90% of patients with breast cancer ultimately discover the disease by themselves regrettably at advanced stages, outside of a structured BSE (3). The INBCRC demonstrated on a sample, representing the educated Iraqi female population, that less than 50% of those who have heard about BSE actually practiced the maneuver. The most common reason recorded   by those who did not was the lack of knowledge on how to perform BSE correctly (13, 14)

Educational information on BSE can be accomplished utilizing commonly available pamphlets, instrumental video tapes or one-to-one personal teaching by a physician or a nurse. The freely offered screening services, seminars and public health educational material by the aforementioned Iraqi National Programs have consequently supported spreading the information about BSE locally. Endorsing such initiatives through urging media network to advertise freely on that topic could encourage the lay Iraqi woman to direct her attention to the significance of BSE in detecting a lump at its earliest stage. The term "breast awareness" is used to describe a woman's familiarity with her breasts

The best time to perform BSE is after the end of menstruation; more specifically 7-10 days from the start of the menstrual cycle; when the breasts are less engorged or tender. For pregnant and postmenopausal women, it is recommended to localize a certain day in each month. If the woman is lactating, BSE should be carried out after evacuating the milk.

Procedure of BSE (15, 17a):

Inspection: Recommended Steps (Figure 2)

1- Look thoroughly at both breasts in front of a mirror with her shoulders straight and arms on the hips searching for any abnormal signs as described above,
2- Raise the arms overhead or put the hands behind the head andlook carefully for the same changes.
3- Put her hands on the middle of the abdomen and push downward with the shoulders stretched forward to look for the shape of the breasts.
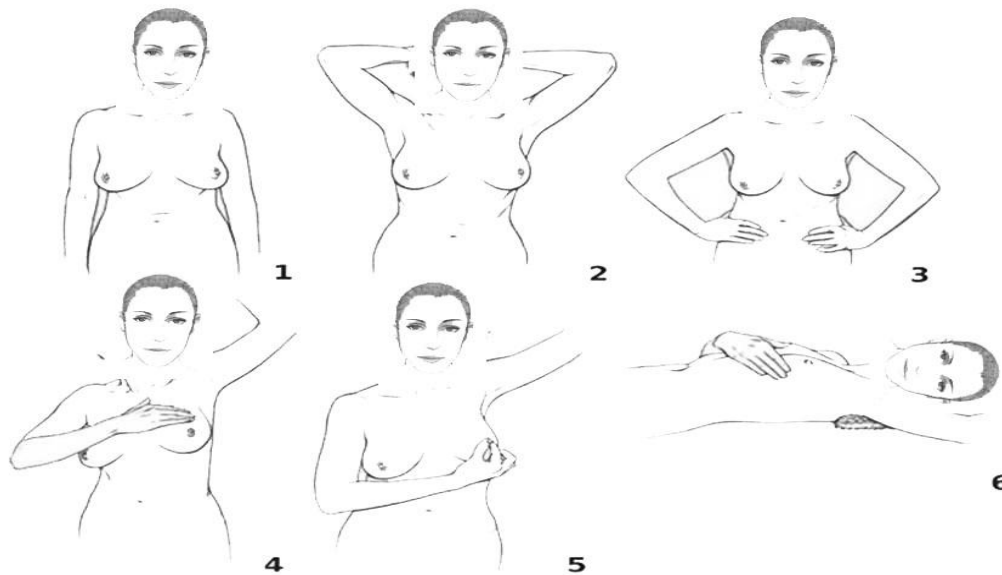
Figure (2): Procedure of BSE

Palpation: Recommended Steps

4- Feel each breast separately using the palmer aspect of the hands in a systemic fashion; searching for any abnormal thickening, irregularities or lumps. Fingers should move in concentric, vertical or radial patterns to reach the tail of the breast and the armpit (axilla). Powder or soap solution might allow fingers to slide smoothly over the skin.
5- The nipples .should be squeezed gently to check for any abnormal discharge.
6- Lie down with a pillow under the right shoulder and place the right arm behind the head. Check the entire breast and armpit area using the finger pads of the left hand and vice versa.

Recommendations:

In Iraq, in view of the relatively high prevalence of breast cancer in younger age groups and due to the late stage at presentation, Iraqi females are advised to perform BSE once each month, beginning at the age of 20 and to continue each month throughout life.

Imaging Techniques:

⬩ Mammography:

This is an X-ray study of the breast utilized since 1940. Mammography is the only proven gold-standard method for detecting non-palpable (occult) cancers as well as "Minimal" breast cancers. Included within the latter category are the lobular carcinoma in situ, non-invasive intraductal carcinoma and minimal invasive carcinoma with a mass no greater than 0.5 cm. in diameter. Modern mammogram equipment uses very low levels of radiation, on average a total dose of about 0.4 m Sv for a typical mammogram with 2 views of both breasts. In general, it is believed that ionizing radiation increases the risk of breast cancer development after a latent period of 10 years and that the risk is cumulative; greatest in adolescent exposure and decreases with increasing age (10, 22-24).

The technique requires compression of the breasts between 2 plates for a few seconds to flatten and spread the tissue. The typical picture of breast carcinoma is an irregular specular opacity and tiny calcifications, with a retraction and thickening of the overlying skin. The mammogram in younger women is less sensitive and usually

difficult to interpret, in view of the denser breast tissues which contain more glands and ligaments, thus obscuring the cancerous tissues (25).

In general, about 10% of diagnostic mammograms are false negatives, with approximately twice that rate for younger women and half that rate for woman over age 65 years. False negative mammograms should be very low especially if quality assurance programs are instituted. The most common causes include dese breast density, rapid growth rate of the tumour, improper positioning of the breast or interpretation errors. While mammograms have a relatively high sensitivity, the specificity of the examination may be inadequate, requiring additional special views, examination by US and tissue biopsies (23-25).

Digital Mammography is currently promoted as an alternative to the traditional mammography; where the image receptor used in conventional mammography is replaced by a digital receptor. The imaging techniques in both remain the same, as breast compression and positioning are unchanged. Digital mammography has the potential to provide images with lower doses of radiation than screen-film mammography.

Mammography Reporting Systems (24, 25):

In our practice, all patients over 40 years are examined by mammography using Full-Digital Mammography, GE Medical System, US (Senographe®) including both mediolateral oblique and cranio-caudal views. All cases are categorized according to **ACR/BI-RADS** Atlas Lexicon by skilled radiologist into 6 categories:

- **BI-RAD 0**: Incomplete study needs supplementary assessment
- **BI-RADS 1**: Normal mammographic study.
- **BI-RADS 2**: Benign lesions requiring routine screening.
- **BI-RADS 3:** Probably Benign lesions; indicating the need for short interval follow up mammgraphy.
- **BI-RADS 4**: Suspicious lesions; requiring fine needle aspiration cytology FNAC or CNB.
- **BI-RADS 5:** Highly Suggestive of Malignancy; recommending FNAC or biopsy followed by appropriate actions, i.e., lumpectomy or mastectomy.
- **BI-RADS 6**: Known Case of Malignancy needs; recommending short interval mammography and appropriate management according the results of tissue biopsy.

Figure (3): Technique of Mammography.

There is sufficient evidence that screening women aged 50–69 years by mammography alone is effective in reducing 25% of mortality from breast cancer (23).

Steriotactic Needle Biopsy of Mammographically Detected Breast Lesions:

For studying impalpable lesions revealed by mammography, a stereotactic technique of needle aspiration is practiced The patient is placed prone on a special table, whereby the breast is positioned in an aperture in the table top and held in a stereotactic compression device that allows stereoradiographs to be taken with a superimposed coordinate system. An instrument holder fitted with a cannula 1.mm. thick and an internal stainless steel screw needle is then attached to the device. The cannula is inserted into the breast tissue allowing sampling; after which a small piece of stainless steel suture thread is introduced into the lesion to serve as a marker for later surgical identification (25, 26).

Recommendations for Mammography Screening:

The Americal College of Radiologists (ACR) (24) recommends annual screening mammography to start at:

- ✓ age 40 years for the general population.

- ✓ age 25-30 for BRCA1 carriers and untested relatives of BRCA carriers.
- ✓ age 25-30 or 10 years earlier than the age of the affected relative at diagnosis for women with a 1st-degree

relative with premenopausal cancer
- ✓ 8 years after radiation therapy but not before age 25 for women who received mantle radiation between the ages of 10-30 years
- ✓ any age for women with biopsy-proven lobular neoplasia, atypical ductal hyperplasia, ductal carcinoma in situ or invasive cancer

The decision to stop mammography screening should be individualized based on the potential benefits and risks of in the context of the overall health status.

In Iraq, as breast cancer is more commonly diagnosed in premenopausal women, it is advisable to start screening mammography at the age of 40 years. After that age, annual screening is recommended. In High Risk groups, screening by mammography should be carried out annually, together with US, starting at the age of 30 years to be continued throughout life.

Ultrasonography (US)

US images are produced from reflected high-frequency sound waves, without exposure to ionizing radiation. It is used primarily to differentiate between solid and cystic masses, to diagnose suspicious axillary nodes, to explore a palpable abnormality not clearly visible on a mammogram or to obtain a better view of a lesion that cannot be mammogrammed. Although US are not accurate in detecting microcalcifications, nevertheless, they can be used to guide aspiration or needle localization (4, 10, 17, 23).
In our practice, breast examination by US is performed using Acuson X300 Ultrasound machine (Siemens, Germany) with high frequency linear array 7.5-10 MHz transducer. Standardized acquisition protocol is used in the scanning techniques. The lesions are categorized according to BIRADS lexicon (that was established by ACR in 1999 and updated in 2003) into 6 groups according to the degree of suspicion; Group 5 indicating "Highly Suggestive of Malignancy" while Group 4 corresponds to a "Suspicious lesion" which recommends ultrasound-guided FNAC or CNB examination.
Recommendations:

It is internationally accepted to screen by US in younger females and high-risk patients who cannot tolerate MRI; justifying its utility in conjunction with mammography when the detected lumps are difficult to be evaluated by mammography alone (4, 10, 16, 22-24).
In Iraq, US is extensively practiced in our Specialized Early Detection Breast Cancer Centers and Clinics, at all age groups, to characterize suspected lesions; specifically in young and premenopausal patients. It is also used as an adjunct to mammography screening in women after the age of 40 years.

Magnetic Resonance Imaging (MRI)

MRI uses magnetic fields instead of x-rays to produce very detailed, cross-sectional images of the body. The sensitivity of MRI as screening tool for breast cancer is over 95% but its specificity is low, with a range of 53%-70%; the higher false-positive rate, results in more call-backs and biopsies. Although low specificity and high cost of MRI restricted its use in routine screening, it has been increasingly used in the screening of high-risk individuals to rule out malignancy in patients with non-palpable lesions and to exclude local recurrence (24-26). The ACR (24) recommends screening with both mammography and MRI to rule out cancer in women who are known (or likely) to have an inherited predisposition to breast cancer.

Biopsy Techniques:

Fine Needle Aspiration Cytology (FNAC):

In general, the definitive diagnosis of a breast mass can be established by: open biopsy, tissue core needle biopsy (CNB) or (Tru-cut) and FNAC. FNAC provides many advantages to the surgeons; being an easy, reliable, inexpensive diagnostic technique which can give rapid results. The procedure could be performed in an office setting without anaesthesia. It is usually not more painful than a venipuncture and can be repeated immediately if the acquired material is inadequate (5, 19, 27).

Technique of FNAC:

When reduced to its simplest terms, FNAC consists of:

- ✓ Using a needle and syringe to remove material from a mass.
- ✓ Smearing it on a glass slide.
- ✓ Applying a routine stain.
- ✓ Examining the specimens under the microscope.

The skin over the palpable mass should be sterilized with an antiseptic. Utilizing the index and the middle finger or the thumb and the index finger, the mass is localized with the non-dominant hand. With firm downward pressure on the skin over the mass, it should be compressed against a rib and stabilized. Aspirates should be obtained using preferably a 22 or 23 gauge, 1 ½ inch disposable needle mounted on a 10 ml plastic syringe, held by the dominant hand. Without using anesthesia, the needle should be gently introduced through the skin passing to the level of the dominant mass. Negative pressure should be created within the syringe by pulling back the plunger. The needle should move back and forth through the mass, in different rotational directions using sewing-like-motion, for at least 6-8 times. All suction should be released before removing the needle from the mass. To limit haematoma formation from the site of the puncture, firm pressure should be applied with a piece of cotton for two minutes. The aspirated material should be immediately smeared on glass slides and dipped in absolute ethanol for fixation for at least 20 minutes. The smeared slides should be then subjected for staining with Papanicolaou stain or H & E.
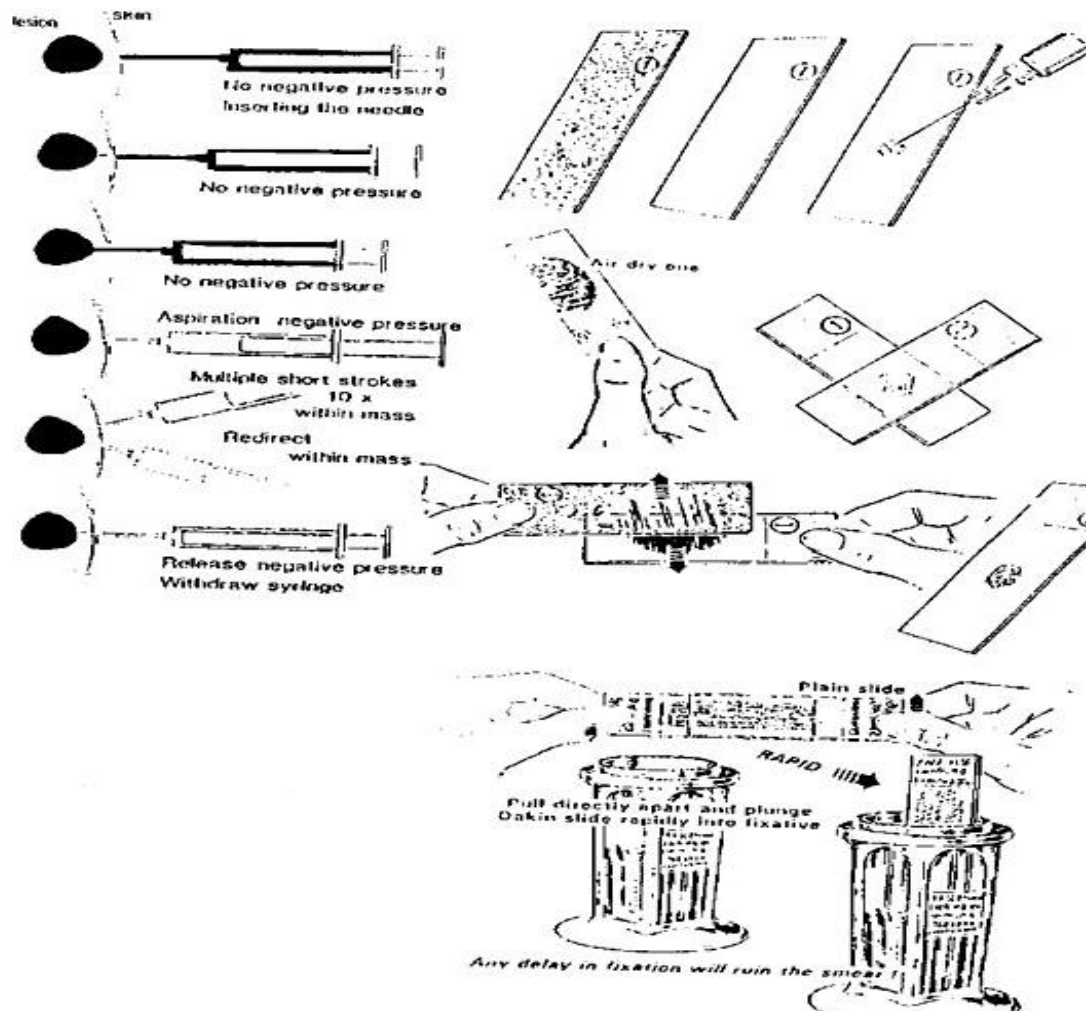

Figure (4): Technique of FNAC and Slide Preparation

Reporting Diagnostic Categories of FNAC (19, 27):

The pathology results of the FNAC or CNB specimens are categorized into:

1. Insufficient aspirate or tissue; requiring a repeated test
2. Benign Breast Disease
3. Atypical/Indeterminate in High Risk lesions; i.e., atypical Fibrocystic Changes, atypical ductal or lobular hyperplasia or lobular carcinoma in situ (CIS).
4. Suspicious for Malignancy
5. Malignant Breast Diseases; i.e., carcinoma in situ, and invasive breast cancer.

Accuracy:

The accurate diagnosis demands the availability of competent cytopathologists; skilled in aspiration and interpretation of the findings and well trained cyto-technicians to ensure the preparation of quality smears. FNAC and CNB should not be performed before the application of the requested screening imaging techniques; as a resulting hematoma can mask the view leading to interpretation errors. False positive diagnoses in FNA cytology occur at a rate of less than 1%, and are frequently due to difficulties with interpretation. False negative diagnoses, on the other hand, are more common, estimated to fall between 3% and 24%; the most common reasons are sampling errors. Atypical cytological findings should not be reported in more than 3-5% of the examined specimens (3, 5, 18, 19, 27).

In general, pitfalls to reliable results from FNAC include aspiration from a vague or small mass (less than 1 cm in diameter) without imaging guide, failure of the aspirating needle to reach a deep seated lump, gross blood into the syringe (i.e., smears coated by RBCs that mask the view), inadequate specimens bearing scanty cellularity; specifically in cases of dense sclerotic lesions and infiltrative lobular carcinomas (19, 27).

Recommendations for FNAC:

The BHGI guidelines (18) recommend FNAC in diagnosing breast cancers in countries with limited resources as a most cost-effective method of obtaining tissue specimens. In metastatic cancer, it could enable the initiation of treatment if malignancy is confirmed in lymph nodes by FNAC. Nevertheless, FNAC does not enable the cytopathologist to distinguish between carcinoma in situ (CIS) and invasive cancers (19).

In our routine practice, FNAC is indicated in the following clinical situations:

- ✓ *Investigation of palpable masses, regardless of their nature*
- ✓ *Investigation of impalpable image-detected masses*
- ✓ *Investigation of suspected local recurrence of breast cancer*
- ✓ *Evaluation of cystic lesions with atypical imaging feature*
- ✓ *Confirmation of a diagnosis of cancer*
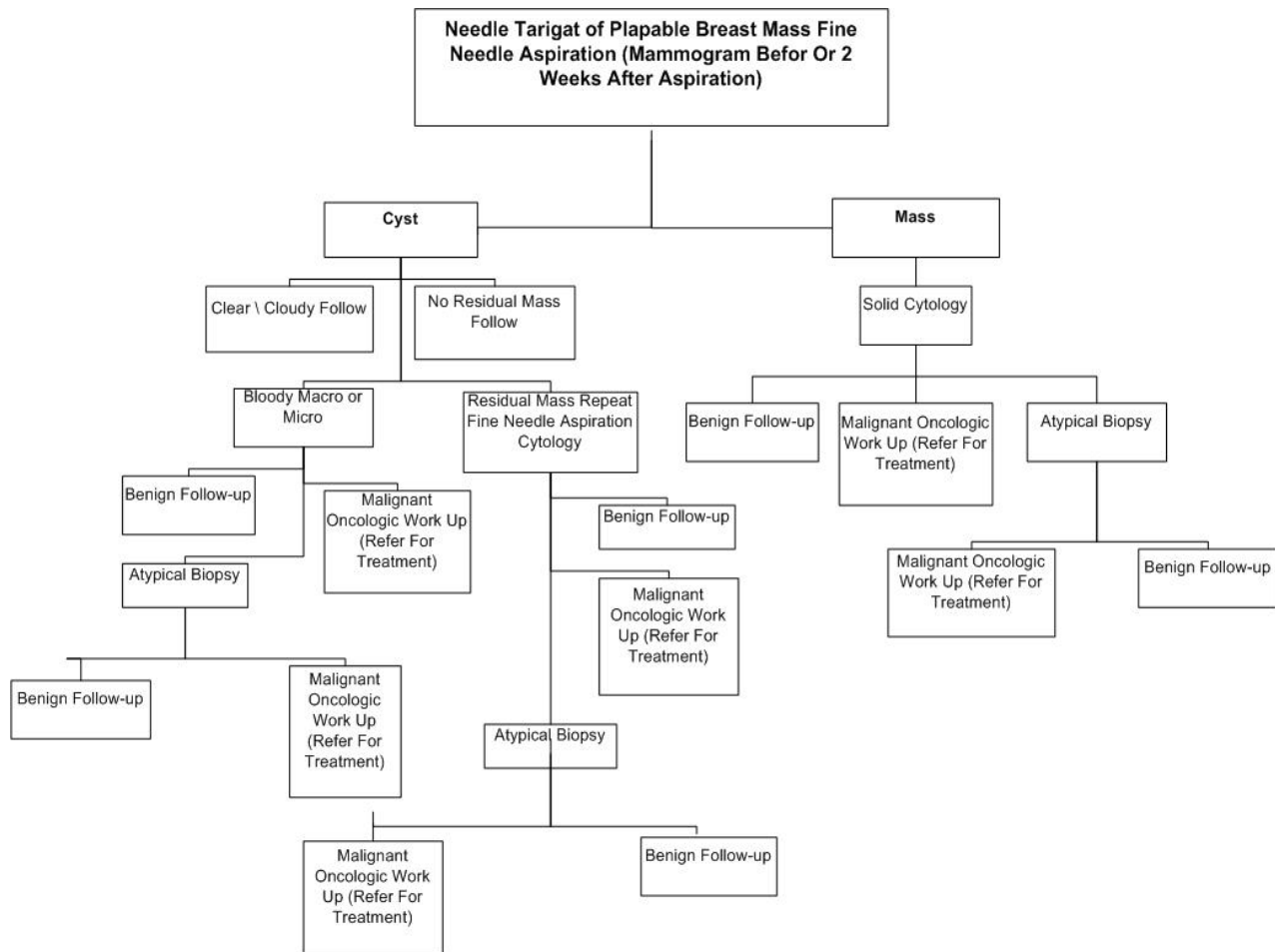
Figure (5): Management of Palpable Breast Lumps Using FNAC

✦ Tissue Core Needle Biopsy (CNB) (19, 27):

In this procedure, larger gauge needles (18-14) are utilized to remove a piece of tissue from the breast lump. It provides a specific histological diagnosis which could be interpreted by a general pathologist. Compared to FNAC, CNB or Tru-cut biopsy is a more traumatic procedure which should be performed under local anaesthesia. It requires more time and special equipment that are more expensive. Pain, discomfort, bleeding and hematoma are common complications.

It is superior to FNAC in the evaluation of suspicious lesions and in cases of microcalcification.. When a patient presents with signs and symptoms of a locally advanced disease, CNB is preferred for the definitive diagnosis of invasive cancer. It is easier to test for the availability of routine hormone receptor status of the tumour using CNB specimens; in FNAC samples cell block material is requested.

It is important to ensure that there is agreement between the imaging appearance and the biopsy results. If the findings are not concordant or if any abnormality is found on the CNB examination, excisional tissue biopsy will be required to ensure an accurate diagnosis. Both FNA and CNB are reported to have rather similar sensitivity and positive predictive values.

Triple Assessment Diagnostic Test and Multidisciplinary Team Approach:

The majority of breast cancers are diagnosed pre-operatively on the basis of Triple Assessment; which depends on the findings obtained from CBE, Imaging studies (Mammograpgy /US) and FNAC (&/0r CNB), as alternative to surgical excision, to confirm a diagnosis of a " Benign" breast lump. The Triple Test can identify the mass as "Cancer" if all the 3 diagnostic modalities indicate malignancy (18, 19, 27, 28):

Accurate interpretation and management of the results of the Triple assessment Test requires a close working relationship between the managing surgeons, the radiologists, the pathologists and the oncologists. If the lesion cannot be visualized on mammogram or if the FNA contains insufficient cells for diagnosis, the triple test cannot be confirmatory.
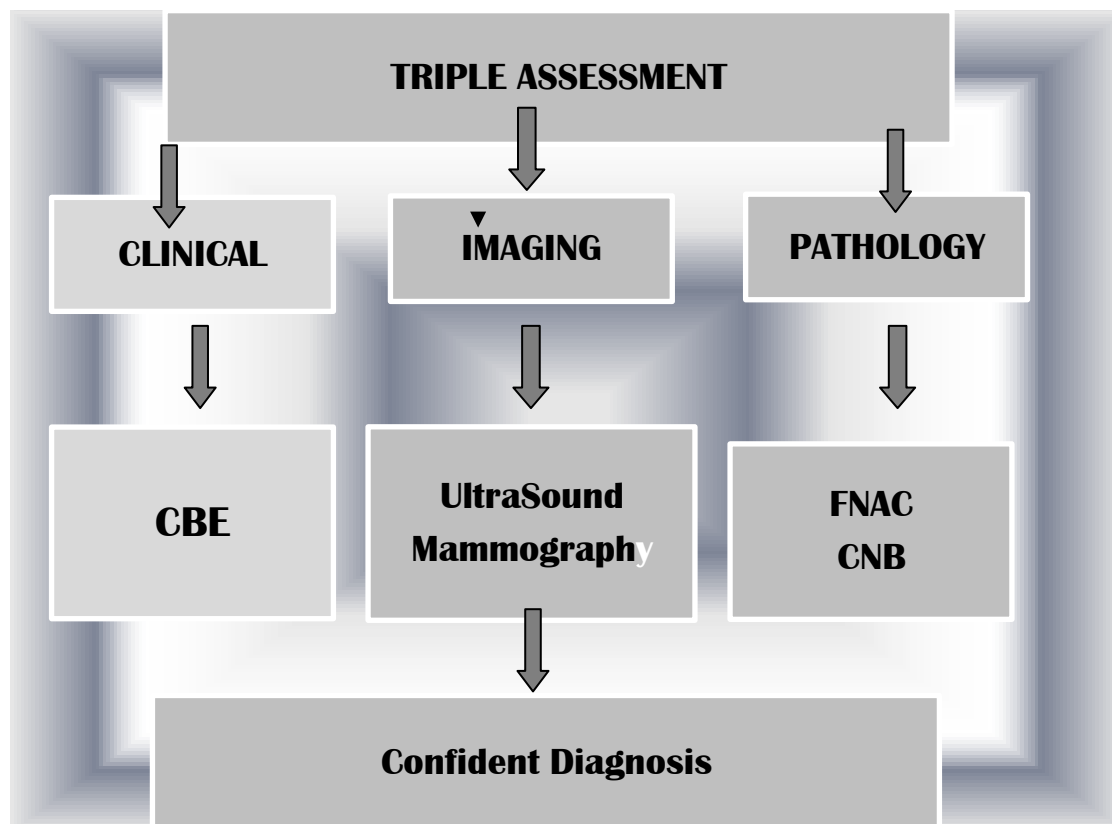

Figure (6): Triple Assessment Diagnostic Test

Breast Cancer Screening in High Risk Women

There are a proportion of women who have a higher risk of developing breast cancer than others. Those include:

- ➢ Women who have personal history of breast cancer (specifically premenopausal breast cancer in a first degree relative).
- ➢ .Women who have history of other premalignant breast lesions (eg, atypical ductal or lobular epithelial hyperplasia).
- ➢ Women who have mutations in BRCA1 and BRCA2 genes.
- ➢ Women who had been exposed to radiation during early years of life especially in the chest region.
- ➢ Women with very dense breast tissues.

In these High Risk Groups, the following early detection approaches are recommended:

➢ BSE should be practiced monthly starting from the age of 20 years to be continued throughout life.
➢ CBE should be performed annually beginning at the age of 20 and continued throughout life.
➢ Screening Mammography should be carried out annually starting at the age group 30-39 years (and in some very high risk groups, i.e., BRCA 1 carriers, at the age group 25-30 years); together with supplementary screening US; to be continued throughout life.
➢ Ultrasound examination is recommended annually starting from the age of 25 years..

Serious Breast Complaints with Clinical Signs and Symptoms:

• Lumps, hard knot or thickening in the breast or axilla
• Swelling, warmth, redness or darkening of the breast
• Changes in the size or shape of the breast
• Dimpling or puckering of the skin over the breast
• Itching, eczematous changes or crust in the area of the nipple
• Retraction or inversion of the nipple
• Nipple discharge that starts suddenly, specifically if bloody
• Persistent recent pain in one area of the breast.

A. For Low Risk Women				
Test	**Age (in years)**			
	20 - 29	**30 -39**	**40 - 49**	**≥ 50**
BSE	Monthly	Monthly	Monthly	Monthly
CBE	Every 2- 3 years	Annually	Annually	Annually
Mammogram	---------	---------	Annually	Annually
B. For High Risk Women				
Test	**Age (in years)**			
	20 - 29	**30 -39**	**40 - 49**	**≥ 50**
BSE	Monthly	Monthly	Monthly	Monthly
CBE	Annually	Annually	Annually	Annually
Mammogram (US)	(Annual US starting at the age of 25)	Annually (with US)	Annually	Annually

Figure (7): The Recommended Schedule for Early Detection of Breast Cancer among Iraqi Females

Referral Guidelines for Primary Health Care Practitioners:

*It is advisable to refer the following conditions to the Secondary or Tertiary Health Care Hospitals/Centers for further evaluation (*28):

⁂ Lump:

- Suspicious painless mass or masses in the breast or axilla; specifically when it is clinically hard, irregular or fixed.
- Persistent asymmetrical lumps in one or both breasts.
- Abscess formation
- Recurrent Cysts that refill after aspiration.

⁂ Nipple Discharge:

- Blood stained discharge, specifically when unilateral.
- Spontaneous discharge that is stains clothes

⁂ Skin Changes:

- Ulceration, excoriation or scaling
- Dimpling or puckering
- Swelling, redness or continuous tenderness
- Abnormal vascularity

⁂ Nipple Changes:

- Itching, eczematous changes or crust in the area of the nipple
- Retraction or inversion of the nipple
- Change in the original direction

⁂ Pain:

Continuous pain not responding to anaelgesia..

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